Translation

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

| Applicant's or agent's file reference | FOR FURTHER ACTION | See Form PCT/IPEA/416 |
|---|---|---|
| FP2655PCT | | |
| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
| PCT/JP2004/001498 | 12.02.2004 | 12.02.2003 |

International Patent Classification (IPC) or national classification and IPC

A61K 31/195, 31/216, 31/405, A61P 31/12, 1/16, C07C 235/28, 235/76, 237/22, 251/38, C07D 209/20

Applicant

CHUGAI SEIYAKU KABUSHIKI KAISHA

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

3. This report is also accompanied by ANNEXES, comprising:

   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:

      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).

      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☐ | Box No. II | Priority |
| ☐ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☒ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

| Date of submission of the demand | Date of completion of this report |
|---|---|
| Name and mailing address of the IPEA/ | Authorized officer |
| Facsimile No. | Telephone No. |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/JP2004/001498

**Box No. I Basis of the report**

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☒ the international application as originally filed/furnished

☐ the description:

pages _____ as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☐ the claims:

nos. _____ as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☐ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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**Box No. IV Lack of unity of invention**

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
   - ☐ restricted the claims.
   - ☐ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted the claims nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:
   - ☐ complied with.
   - ☒ not complied with for the following reasons:

The compounds that are set forth in Markush form in claim 15 can be considered to have a common chemical structure wherein prescribed substituent groups have been bonded to a citric acid amide, as is set forth in general formula (I). However, compounds which have the structure in question are well known, as disclosed in the document EP 1002793 and the like; therefore, this chemical structure cannot constitute a distinguishing element of the overall chemical structure. In addition, there is no other common feature that can be considered to be a special technical feature in the meaning of the second sentence of PCT Rule 13.2 among these groups of inventions. As a result, the groups of inventions in question cannot be considered to be so linked as to form a single general inventive concept.

4. Consequently, this report has been established in respect of the following parts of the international application:
   - ☒ all parts.
   - ☐ the parts relating to claims Nos. _____

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**Box No. V** **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Claims | 1-14, 19, 20, 22-24 | YES |
| | Claims | 15-18, 21 | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-24 | NO |
| Industrial applicability (IA) | Claims | 1-24 | YES |
| | Claims | | NO |

2. Citations and explanations (Rule 70.7)

Document 1: Tetrahedron Letters, 1998, Vol. 39, No. 8, pages 877 to 880

Document 2: EP 1002793 A1 (Takara Shuzo Co., Ltd.), 24 May 2000

Document 3: EP 526936 A2 (Merck and Co., Inc.), 10 February 1993

Document 4: WO 94/18157 A1 (Merck and Co., Inc.), 18 August 1994

Document 5: Journal of Virology, 2002, Vol. 76, No. 20, pages 10465 to 10472

Document 6: WO 93/24660 A1 (The Regents of the University of California), 09 December 1993

[1]

The inventions that are set forth in claims 15 to 18 and 21 lack novelty and do not involve an inventive step in the light of documents 1 to 4 cited in the international search report.

Document 1 indicates that the compounds which are included within the scope of the formula that represents Viridiofungin A(2) exhibit an activity whereby they inhibit squalene synthase.

Therefore, the inventions that are set forth in

claims 15 and 21 of the present application lack novelty in the light of document 1.

Document 2 (claim 1) discloses compounds that are represented by general formula (A), and indicates that said compounds are useful for the treatment of mycotic infections and immunological diseases.

Therefore, the inventions that are set forth in claims 15 to 18 and 21 of the present application lack novelty in the light of document 2.

Document 3 (claim 1) discloses compounds that are represented by general formula (I), and indicates that said compounds are useful for the treatment of mycotic infections and immunological diseases.

Therefore, the inventions that are set forth in claims 15 and 21 of the present application lack novelty in the light of document 3.

Document 4 (claim 1) discloses compounds that are represented by general formula (I), and indicates that said compounds are useful for the treatment of mycotic infections and immunological diseases.

Therefore, the inventions that are set forth in claims 15 and 21 of the present application lack novelty in the light of document 4.

[2]

The inventions that are set forth in claims 1 to 14, 16 to 20 and 22 to 24 do not involve an inventive step in the light of documents 1 to 6 cited in the international search report.

Claims 1 to 14

Documents 3 and 4 disclose compounds that are

represented by general formula (I), and makes disclosures in relation to the farnesyl transferase-inhibiting action of said compounds; however, documents 3 and 4 do not make any disclosures pertaining to the application of the compounds in question in relation to viral infections such as HCV. On the other hand, document 5 indicates that farnesyl transferase inhibitors are useful for the treatment of viral infections, and document 6 further indicates that medicinal agents which exhibit a prenylation reaction-inhibiting action are useful in the treatment of viral infections such as HCV.
Conventionally, if the activity of farnesyl transferases is inhibited, then prenylation reactions will also be inhibited; therefore, it would be easy for a person skilled in the art to conceive of attempting to employ the farnesyl transferase inhibitors that are disclosed in documents 3 and 4 for the treatment of viral infections such as HCV.

Claims 16 to 20 and 22 to 24

It would be easy for a person skilled in the art to attempt to create specific citric acid amide compounds by selecting the substituent groups from various citric acid amides that are useful as medicinal agents, as appropriate. In addition, it would be easy for a person skilled in the art to conceive of attempting to employ the resulting compounds for the treatment of viral infections such as HCV in the light of the disclosures of documents 5 to 6.

**Box No. VIII** **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Scope of the Search

Claims 1 to 24 include a very wide range of compounds, which are indicated by the term "prodrugs," as the active ingredient. However, only an extremely small portion of the claimed compounds is disclosed in the meaning of PCT Article 5; therefore, the claims in question are not fully supported in the meaning of PCT Article 6.

Furthermore, the preceding international search report was drafted on the basis of a search of prior art documents in relation to the compounds that are specifically set forth in the description; therefore, the present international preliminary report on patentability has been drafted in relation to the subject matter that was included within the scope of the search in question.